Knowledge Acquisition Session Report
NCI – DCP Protocol Information Office

KA Session Date: May 12, 2000 **Time:** 9:00 – 10:30 A.M.

Session Topic: DCP Drug Supply Procedures; Chemopreventive Agent Repository

Knowledge Analysts: Bill McCurry, ScenPro, Inc.; Lisa Chatterjee, Oracle.

Organization: Protocol Information Office, NCI Division of Cancer Prevention

Session Location: Rockville, Maryland

Type of Session:

_____ Interview _____ Task Analysis _____ Scenario Analysis
____ Concept Analysis _____ Observation _X_ Structured Interview
_____ Other:

Documentation: KA Session Report

General Topic Area

Division of Cancer Prevention – Clinical Study Drug Supply Procedures.

Session Objective

To document the McKesson Chemopreventive Agent Depository's role in the Division of Cancer Prevention's mission.

Report Summary

McKesson HBOC maintains a CAR (Chemopreventive Agent Repository) to meet DCP's (Division of Cancer Prevention) clinical study drug supply needs. CAR personnel receive bulk drug material shipments and calculate the needed drug supply based on protocol information. CAR personnel then package, label, and store the drug supply. The CAR ships the drug supply to site pharmacies as needed for the studies. CAR personnel also solicit competitive bids for agent formulation and packaging on large studies. Six to eight weeks is the ideal lead time for work that the CAR can perform in-house, but competitive bids can require more than six months. CAR's internal drug supply information management system does not interact with any DCP systems. The initial version of DCP's PIMS (Protocol Information Management System) will not provide this link, but a later version may. DCP has attempted to stimulate chemoprevention research. This has resulted in a flexible approach to working with the cancer research community, based on strong working relationships between DCP personnel and researchers.

McKesson Chemopreventive Agent Repository

McKesson HBOC, Inc. holds the drug supply management contract with the NCI Division of Cancer Prevention (DCP). McKesson employs almost 25,000 people worldwide in three core businesses: supply management, pharmaceutical services, and information technology. McKesson maintains a Chemopreventive Agent Repository (CAR) in Rockville, Maryland to serve DCP's drug supply needs. Greg Bullard, McKesson Principal Investigator, manages the CAR.

CAR Involvement in the Clinical Study Process

The CAR provides drug supply services at several points after DCP receives a protocol. Figure 1 on the following pages depicts the Repository's involvement with DCP clinical studies.

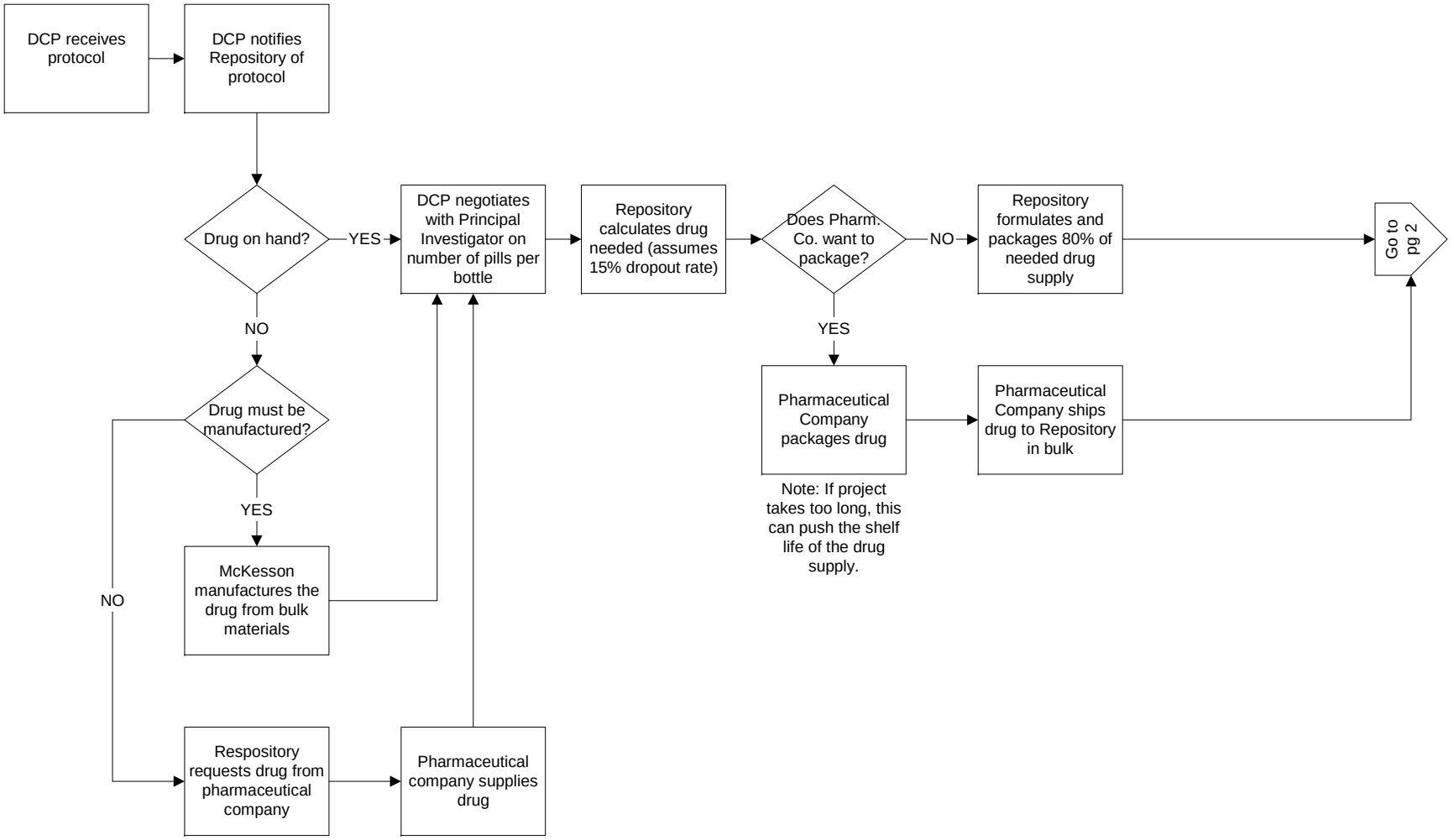

Figure 1: DCP Clinical Study Drug Supply Process

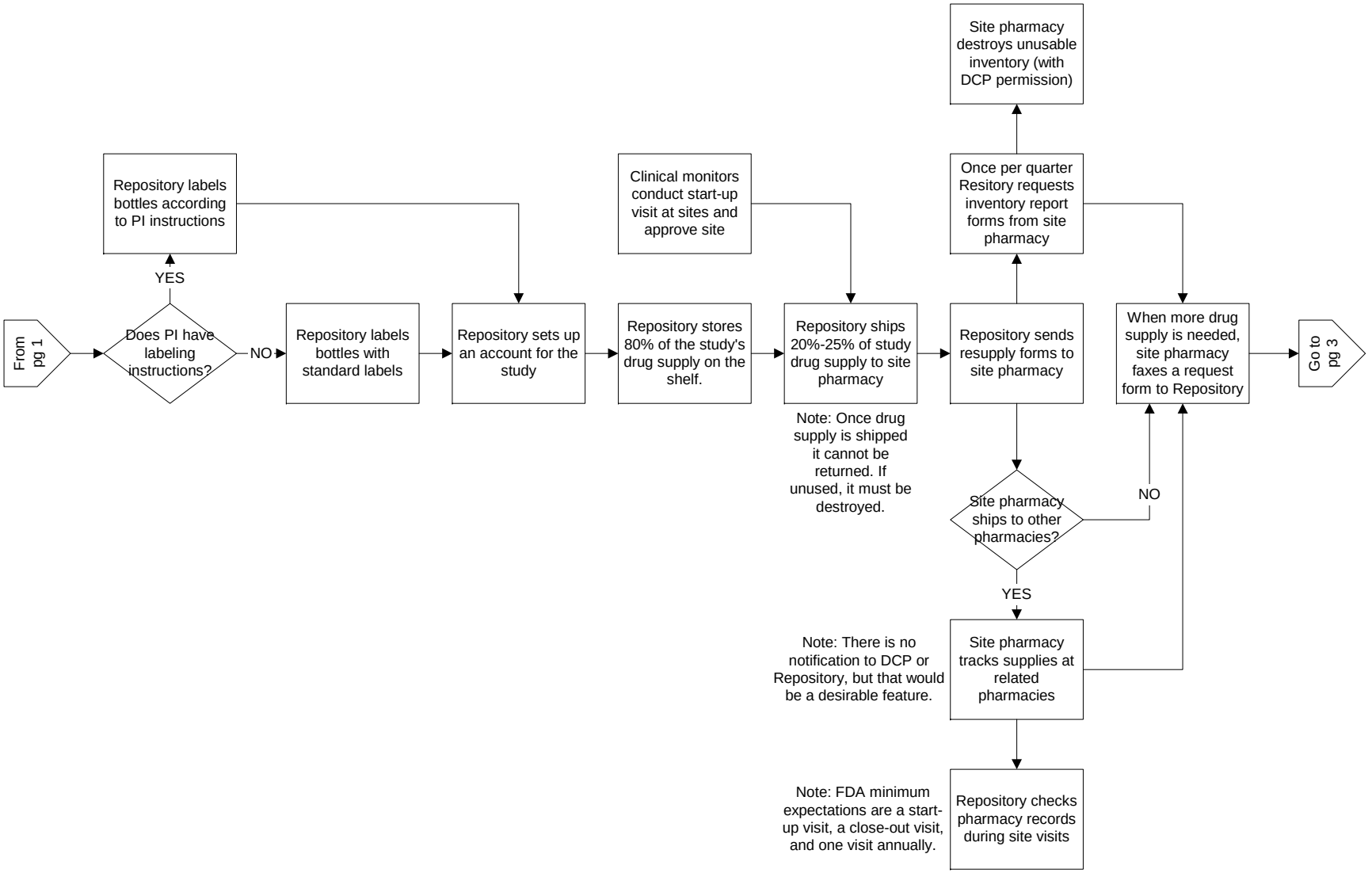

Figure 1: DCP Clinical Study Drug Supply Process (continued)

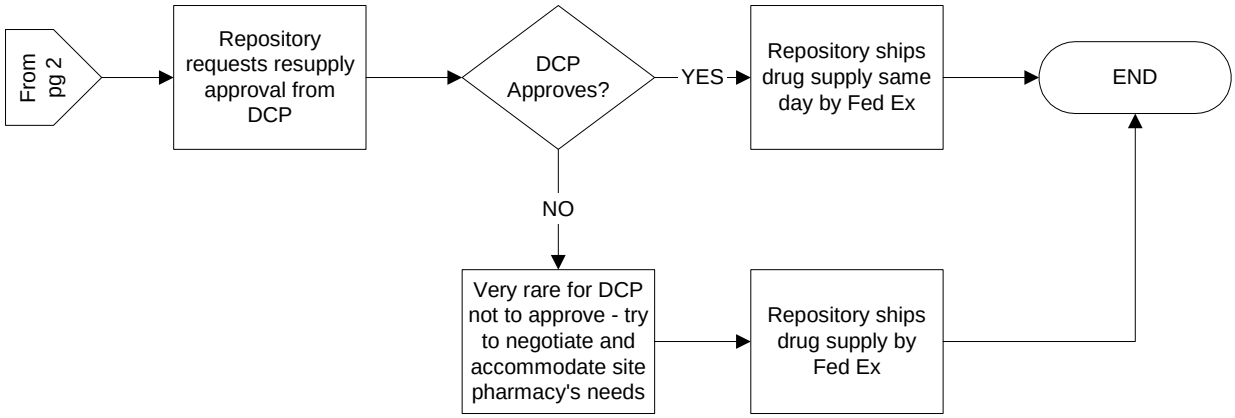

Figure 1: DCP Clinical Study Drug Supply Process (continued)

The CAR personnel receive and log shipments from pharmaceutical companies. Sometimes these shipments contain prepackaged drugs, and sometimes they contain of bulk clinical agents. CAR personnel store these materials until they are needed for a DCP protocol.

DCP personnel inform the CAR personnel of upcoming protocols. CAR personnel then determine whether the required drug is on hand. If the drug is not on hand, the CAR personnel may need to request drug supply from the pharmaceutical company. In other cases, the CAR must arrange to manufacture the drug. CAR personnel solicit bids for contracts to manufacture drugs. The bid and evaluation process may require six months to a year.

Many chemopreventive agents are expensive. Drug supply that has been shipped to a study site and then not used must be destroyed. DCP may require site pharmacies to ship unused drug supply back to the CAR for destruction, or DCP may allow a site pharmacy to destroy unused drug supply. The CAR has introduced several procedures to minimize drug supply waste. These procedures include:

- preparing or securing only eighty percent of the drug supply needed for a study before the study begins
- labeling procedures that allow packages of drugs to be reassigned to another patient if the original patient drops out
- limiting initial study site shipments to about twenty-five percent of the drug supply needed for a study

Principal investigators, pharmaceutical companies, and study site pharmacies will sometimes make specific requests that preclude these waste minimization procedures. DCP and CAR will negotiate with the requesters in these cases, but they frequently comply with study-specific requests.

The CAR requires sufficient lead time when it labels drug packages. This process takes four to six weeks.

CAR personnel ship the initial drug supply to a site pharmacy after DCP clinical monitors have conducted a study start-up visit of the site. CAR personnel ship drug supply to site pharmacies, not to individual physicians.

In multi-site studies the CAR will ship to the main site pharmacy and allow it to distribute drug supply to the related site pharmacies. The main site pharmacy is responsible for tracking drug supply

at the related site pharmacies. CAR personnel will check this tracking when performing site visits and audits. Dr. Crowell felt that multi-site studies are a trend that will continue to grow.

The CAR also sends the main site pharmacy resupply forms. When the site pharmacy needs additional drug supply, its personnel will fax a request form to CAR. CAR personnel will request resupply approval from DCP personnel in the Chemopreventive Agent Development Research Group. Approval is almost always given. The CAR then ships drug supply to the site pharmacy the next business day after the request is received.

Once per quarter CAR requests inventory report forms from site pharmacies. Over ninety percent of the site pharmacies send the requested information. This process allows CAR personnel to track usage and drug supply levels for each study in progress.

CAR personnel visit site pharmacies at various times throughout a study. The FDA expects one start up visit, one close out visit and at least one annual visit in between at minimum. If principal investigators have not accounted for the cost of these visits, the study can run over budgeted costs.

CAR Required Lead Times

The amount of lead time required by the CAR depends on the cost of the drug supply involved. For smaller trials costing less than $25,000, the CAR may handle all the work in-house. This requires at least one month notice before the drug supply is needed. A lead time of six to eight weeks is optimal in these cases.

CAR personnel must solicit competitive bids and get contract officer approval when the drug supply cost exceeds $25,000. This process may require six month or more. Starting from scratch to make a clinical formulation requires about one year. The CAR frequently does not get enough lead time to meet the timelines for large clinical trials.

Sometimes the pharmaceutical companies contribute to delays. Pharmaceutical company attorneys may want to see the approved protocol before releasing the bulk drug material. When protocols undergo many revisions, the CAR can receiving the bulk material with little time remaining before the protocol begins accruing patients.

CAR Information Needs

CAR personnel need to know which agent is needed for a protocol, how much is needed, and when it is needed. CAR personnel require the following specific information:

- drug to be used
- dosage
- expected number of patients
- expected date to begin accruing patients
- type of packaging
- amount of drug per package
- labeling required
- randomization codes required
- study sites (location and number)

- instructions for destroying unused drug supply
- authorizing individual
- authorization to ship drug supply

CAR Information Management

The CAR tracks drug supplies with a FoxPro database system on a stand-alone workstation. This system is supplemented with a book in which CAR personnel record incoming material shipments and outgoing drug supply shipments. McKesson's current DCP contract includes one-half of an FTE for creation of a new drug supply information management system.

Some drug supply information is stored in multiple locations within DCP and CAR. Contact names, contact addresses and milestone correspondence are examples of this type of information.

The CAR system does not link directly to any DCP systems at this time. It may be possible for DCP's new Protocol Information Management System (PIMS) to exchange information with the CAR's system. Oracle will not build that functionality into PIMS' initial version, but Oracle may include preparations required for its addition in a later version.

The CTEP-ESYS system includes a Dose Regimen module that manages Cancer Therapy Evaluation Program (CTEP) drug supply information. This system could be used as a template for a drug supply management module in PIMS.

DCP Management of the CAR

Dr. Crowell has managed the CAR in addition to his other duties as a Program Director in the DCP Chemopreventive Agent Development Research Group. On July 2, 2000 Izet Karpetovich will take over full time management of the CAR for DCP.

DCP routes all CAR drug orders through Alfred Fallavollita, Chief of the CTEP Pharmaceutical Management Branch PMB. McKesson maintains a drug repository for CTEP also, and PMB personnel frequently send CTEP drug orders to McKesson. Routing DCP drug orders through PMB reduces the confusion that could be caused if many people at NCI were providing direction to McKesson. However, there may be some value in authorizing DCP branch heads to approve DCP drug orders.

Division of Cancer Prevention Approach to Research

The Division of Cancer Prevention (DCP) has been trying to stimulate cancer prevention research. As a result, DCP had been very flexible in working with principal investigators, pharmaceutical companies, and study sites.

Much of DCP's work in stimulating research has been done by building trust and strong individual working relationships between DCP personnel and researchers. As a result, much of DCP's clinical study management continues to hinge on these interpersonal relationships.

Entries for Domain Dictionary

Chemopreventive Agent Repository (CAR): Rockville, Maryland facility operated by McKesson HBOC, Inc. to meet the clinical study drug supply needs of the NCI Division of Cancer Prevention.